Remarks/Arguments

The Examiner has rejected claims 1 - 2 and 29 - 33 under 35 U.S.C. § 103(a) as being unpatentable over Qian (US Patent 6,077,846 ("'846") in view of Krause et al., Kooyman et al., and Schrattenholz et al. The Examiner further rejects claims 34 - 60 as being unpatentable over Qian (US Patent 6,077,846 ("'846") in view of Krause et al., and Kooyman et al.

The Examiner states, "While Qian et al., do not teach the addition of a positive modulator of a nicotinic receptor agonist in the prior art invention, Qian et al., do suggest the use of additional agents in the prior art composition. See USPN '846, col. 10, lines 36 - 40."

First, Applicants respectfully point out that '486 makes no mention whatsoever of nicotinic receptor modulators. US '486 is concerned with nicotinic receptor agonists and particularly with epibatine and derivatives thereof. Accordingly, Applicants respectfully request that the Examiner withdraw and reconsider the rejection. Applicant makes this request on the grounds that the cited art is **not** analogous art as defined by the holdings of the Federal Circuit. As explicated in the MPEP:

> Analogous art depends upon the necessary essential function or utility of the subject matter covered by the claims and not upon what they are called (MPEP § 904.01(c)).

Further, section 2141.01(a) of the MPEP recites a holding of the Federal Circuit as follows:

> "In order to rely on a reference as a basis for rejection of an applicant's invention the reference must either be in the field of the applicant's endeavor or, if not, than be reasonably pertinent to the problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

Applicant respectfully submits that the cited art, namely Qian et al., (U.S. '486), is in the field of art concerned with nicotinic receptor agonists.

In contrast, the present invention is directed to nicotinic receptor modulators which act in a different way, act at different sites and which would be administered for different purposes.

Therefore, Applicant respectfully asserts that the cited reference is **not** in the field of the applicant's endeavor, **neither** is it reasonably pertinent to the problem with which the inventors were concerned.

> Second, the lines in '486, cited by the Examiner state:
> "It should be understood that in addition to the ingredients particularly mentioned above the formulation of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example, those

suitable for oral administration may include such further agents as sweeteners, thickeners and flavoring agents."

Applicants respectfully point out that these lines are properly read in the context of the section of '486, that extends from Col. 8, line 56 through Col. 10, line 42. This entire section of '486 is directed to describing how Qian et al's., active ingredient may be formulated for administration by a variety of routes e.g., oral, nasal rectal, topical, etc., (see Col 9, lines 31-33). At Col. 9, lines 24-25, Qian et al, state, "While it is possible for the active ingredient to be administered alone, it is preferable to present it as a pharmaceutical composition." Indeed, properly construed, the entire section of '486 from Col. 8, line 56 through Col. 10, line 42 is directed solely to teaching the formulation of the active ingredient (epibatine or a derivative thereof) for administration by a variety of routes. Nothing in '486 suggests or provides any motivation for using epibatine or a derivative thereof in combination with any other active ingredient.

Krause, *et al.*, describe what is alleged to be a positive allosteric effect of the antihelminthic compound Invermectin on the α7 neuronal nicotinic acetylcholine receptor. While the information provided by Krause, *et al.*, could be read to suggest the value of searching for allosteric modulators that modulate the activity of α7 neuronal nicotinic acetylcholine receptors, Krause, *et al.*, state at page 293, first column, "The existence of a specific site allowing the binding of an allosteric effector does not necessarily imply the existence of an endogenous natural ligand . . . although IVM may interact with a specific domain of the protein, this drug may cause an allosteric potentiation comparable to that produced by a physiological but yet unknown compound that binds to another site." (underlining added for emphasis). The teaching by Krause, *et al.*, is thus entirely speculative making a search for modulators no more than obvious-to-try. Applicants respectfully submits that nothing in Krause, *et al.*, suggests or makes obvious the compounds of the present invention.

Kooyman, *et al.*, discuss the action of 5-hydroxyindole in 5-HT_3 receptors. Applicant respectfully asserts that the Kooyman, *et al.*, is not in the field of the applicant's endeavor, neither is it reasonably pertinent to the problem with which the inventors were concerned. Accordingly, Applicants take the position that the reference is not properly citable against the present application.

Scrattenholz, *et al.*, provide data that suggest that galanthamine, 1-methyl-galanthamine and 5-hydroxytryptamine can potentiate the responses of neuronal nicotinic acetylcholine receptors to agonists. Applicants can find nothing in Scrattenholz, *et al.*, to suggest that the effect described is truly generalizable, that is whether it applies to all forms of neuronal nicotinic acetylcholine receptors and in particular to α7 neuronal nicotinic acetylcholine receptors. In any event, Applicants respectfully submits that nothing in Scrattenholz, *et al.*, suggests or makes obvious the compounds of the present invention.

Finally, the Examiner has rejected the claims of the present application as being unpatentable over '846, in view of Krause, *et al.*, Kooyman, *et al.*, and Scrattenholz, *et al.* Applicants respectfully submit that a careful reading of the references cited by the Examiner does

not provide support for the three basic criteria that must be met to establish a *prima facie* case of obviousness. The three basic criteria are: First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references where combined) must teach or suggest all claim limitations. (Manual of Patent Examining Procedure, Rev. 2, July 1996 § 2142).

Simply stated, the present invention concerns compounds that have new and different activities not disclosed or taught in any of the references cited by the Examiner when such references are taken alone or in combination. Therefore, Applicant respectfully requests that the Examiner withdraw the rejection of claims one of the present application on obviousness grounds under 35 U.S.C. S 103.

Respectfully submitted

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